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EXAMINER	
MARSCHEL A	

ART UNIT	PAPER NUMBER
1807	9

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-47 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 1-47 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☒ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).

12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 180, Art Unit 1807.

If applicant desires priority under 35 U.S.C. § 120 based upon a parent application, specific reference to the parent application must be made in the instant application. It is noted that this appears as the first sentence of the specification following the title. Status of the parent application (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "Patent No." should follow the filing date of the parent application. If a parent application has become abandoned, the expression "abandoned" should follow the filing date of the parent application.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The title covers methods only whereas the instant claims are also directed to compositions. Also the title is lacking as to the retinoblastoma central aspect of the invention.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

On pages 137-147 of the specification there is described the

detection of chromosome 3/17 aberrations. This is the only disclosure in the specification directed at these chromosomes. The cell lines studied are listed on page 141, first paragraph. None of those cell lines nor the accompanying discussion involve the retinoblastoma gene as claimed in claim 1, for example. Thus there is a complete lack of instant enablement that a chromosome 3/17 rearrangement is associated with the retinoblastoma gene as claimed in claim 1 etc.

Claims 1-28 and 34-45 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1-28, 31, 34-45, and 47 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to retinoblastoma rearrangement detection wherein there is used the specific primers showing chromosomal rearrangements involving chromosomes 13 and 21 as given in Example IX starting on page 130 of the specification. There is no guidance or enablement of involvement of other chromosomes or primers. There is especially no guidance as to what is meant as to the location of "the vicinity" given in claim 1, line 3. Additionally, the reference cited by applicants by Bowcock et al. is enclosed with this office action and summarizes in the abstract that the linkage between the chromosome 13 RB gene and cancer is not clear and may be secondary or present in some tumors only be chance. Thus even the instantly discussed rearrangement is in question as to its enablement. See M.P.E.P.

§§ 706.03(n) and 706.03(z).

Claims 1-21 and 29-38 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-21 and 29-33 are vague and indefinite in that they are supposedly method claims but do not recite even a single positive method step.

Claims 1-21, 31, and 34-38 are vague and indefinite in that they cite a nucleic acid sequence (e.g. claim 1, line 2) as if it was a composition. A "sequence" of a nucleic acid is a characteristic of said nucleic acid and not a composition in itself. Thus citing a sequence as a composition is confusing and unclear as to what is meant. Clarification is requested.

Claims 15-21 and 43-45 are rejected under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claims 15-21 broaden rather than further limit the scope of claim 1 from which each ultimately depends. Claim 1 is limited to probes only for chromosomes 3 and/or 17 and do not cover a scope including other chromosomes. Therefore, the added chromosomes 13 and 21 in claim 15 is not further limiting from claim 1.

The limitations in claims 43-45 do not define a composition that is any more limiting than that of claim 22 from which claims 43-45 depend. The use of probes in kits, dosimetry, and prenatal

testing does not further limit the composition of claim 22.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 8-13, 28, and 33 are rejected under 35 U.S.C. § 101 because they are directed to a cancer detection utility, prognosis, effectiveness of therapy, etc. that must be definite and in currently available form for which evidence is lacking in the instant disclosure. The data in Table 4 on page 135 is insufficient to show said utility clearly due to a lack of controls as well as data directed at diagnostic etc. determination that could be correlated between various samples. See the MPEP § 608.01(p), section on 35 U.S.C. 101.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 29, 30, 32, 33, and 46 are rejected under 35 U.S.C.

§ 102(e) as being clearly anticipated by Weissman et al.

Weissman et al. discloses in columns 5-6, bridging paragraph, that the invention therein described detects chromosomal arrangements such as the spacing between genes including linkage that may be related to a disease. Probed regions are disclosed as 50 kb to 2000 kb in column 9, lines 14-32, which clearly qualifies as high complexity probes as instantly claimed. The coverage of the probed region is accomplished as depicted in Figure 5 (discussed in column 18, lines 32-62) and discussed as to probes prepared in the bridging paragraph between columns 18 and 19. This probe and hybridization practice clearly reads on the above rejected claims.

Claim 29 is rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Yunis et al.

The abstract of Yunis et al., the "Materials and Methods" technique, and the results shown in Figures 3-5 read on the rejected claims in that a method is disclosed where probes that will hybridize throughout the human gene complement show the localization of expressing genes and thus show staining of chromosomes that show differences due to expression between chromosomes as given in claim 29.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not

identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-47 are rejected under 35 U.S.C. § 103 as being unpatentable over Weissman et al.

The instant invention is directed to high complexity probes and their use for hybridization labeling of chromosomes to detect rearrangements that may be associated with various disease states.

Weissman et al. discloses in columns 5-6, bridging paragraph, that the invention therein described detects chromosomal arrangements such as the spacing between genes including linkage that may be related to a disease. Probed regions are disclosed as 50 kb to 2000 kb in column 9, lines 14-32, which clearly qualifies as high complexity probes as

instantly claimed. The coverage of the probed region is accomplished as depicted in Figure 5 (discussed in column 18, lines 32-62) and discussed as to probes prepared in the bridging paragraph between columns 18 and 19. Weissman et al. lacks the specific retinoblastoma rearrangement disclosure but is motivated to study such rearrangements as summarized in column 2, line 13, through column 4, line 5.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice high complexity probes and their use in hybridization assay as instantly claimed because Weissman et al. discloses the method and the motivation to apply this to diseases suspected of being caused by genetic rearrangements such as retinoblastoma gene rearrangements that result in cancer.

Claims 1-47 are provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as that of claims 1-47 of copending application Serial No. 07/659,974. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The disclosure is objected to because of the following informalities:

On page 18, the citation to Waldman et al. is incomplete.

On pages 131, 140, 144 and 145; lines 2, 11, 25, and 11; respectively; the citations are incomplete.

In claim 23, line 1, the word "probves" appears to be misspelled.

Appropriate correction is required.

No claim is allowed.

Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).
The CM1 Fax Center number is (703) 308-4227.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

AM
A. MARSCHEL:am
August 10, 1992

M. Moskowitz
MARGARET MOSKOWITZ
SUPERVISORY PATENT EXAMINER
GROUP 180